American Journal of Medical Genetics 68:240–241 (1997)

Letter to the Editor

Trisomy 18 Mosaicism in a Woman With Normal Intelligence, Pigmentary Dysplasia, and an 18 Trisomic Daughter

To the Editor:

Survival beyond the age of 10 years is rare among 18-trisomic individuals. Most of these long-term survivors, when more than one tissue is studied, are normal/trisomy mosaics. They are usually mentally severely retarded with a variety of anomalies [Murano et al., 1991]. There is another group of mosaic individuals: 7 women and a 13-year-old girl, with a low frequency of 18-trisomic cells, normal or mildly retarded intelligence, and minor anomalies [Beratis et al., 1972; Bensen and Steele, 1985; Kohn and Shohat, 1987; Gersdorf et al., 1990; Graham et al., 1992; Sarigol and Rogers, 1994; Butler, 1994; Collins et al., 1995]. Two of them were diagnosed after delivering malformed stillborn infants [Kohn and Shohat, 1987; Gersdorf et al., 1990]. One of them was the mother of a trisomy 18 patient who was coincidentally found to have trisomy 18 mosaicism [Beratis et al., 1972]. Pigmentary dysplasia, previously called hypomelanosis of Ito, is a disorder with linear, swirly, or patchy, hypo- or hyperpigmented areas of skin, resulting from migration and interaction of melanoblasts of different pigmentary potential. The disorder is often accompanied by mosaic chromosomal abnormalities, including mosaic trisomy 18 [Murano et al., 1991]. Here we report a 26-year-old woman with low frequency trisomy 18 mosaicism, normal intelligence, and pigmentary dysplasia, who gave birth to an 18-trisomic girl.

The proposita was born at term with a weight of 2,310 g to a 33-year-old mother and a 35-year-old father, both healthy and unrelated. Her elder brother is normal. She had recurrent otitis media in infancy that resulted in right severe hearing loss. A cleft lip was repaired. She was high school educated, and worked as a receptionist in a movie theater and then as an insurance sales woman. She married at age 25 years and gave birth to a girl with a low birth weight (1,938 g at 37 weeks of gestation), multiple congenital anomalies, and nonmosaic trisomy 18. The baby died at age 11 months.

Cultured peripheral blood lymphocytes from the proposita documented 47, XX, +18(11)/46, XX(39) mosaicism, and cultured skin fibroblasts (from the perineal skin of unspecified pigmentation obtained on episiotomy) showed 12% (6 out of 50) trisomic cells. Her husband had normal chromosomes. Her next pregnancy was monitored by amniocentesis, which gave a normal female karyotype. The baby born was phenotypically normal, and her cord blood lymphocytes karyotype was all 46, XX.

Now age 26 years, the woman to 151 cm (−1 S.D.). She has a high-arched palate and hyperpigmentation on the right side of the body, with a sharp demarcation in the midline of chest and abdomen (Fig. 1a), and linear hyperpigmented areas on the posterior surfaces of both thighs and legs (Fig. 1b). The latter appear to follow the lines of Blaschko [Thomas et al., 1989; Flannery, 1990; Ohashi et al., 1992]. Otherwise, she does not have the abnormalities usually seen in nonmosaic or mosaic 18-trisomics. In particular, she does not have growth or mental retardation, kyphoscoliosis, asymmetry, bushy eyebrows, bulbous nose with broad nasal root, poor dentition or simple ears, i.e., manifestations of long-term survivors with mosaic trisomy 18. It seems advisable to study the mothers of 18-trisomic children for possible mosaicism when they have mild manifestations. The presence of pigmentary dysplasia, as is the case in the proposita of the family we described, would serve as an indicator for chromosome analysis.

The risk of normal/trisomy 18 mosaic women to have 18-trisomic children is assumed to be high, perhaps up to 50%. It depends on the share of 18-trisomic germ cells in the gonads of these women, information which

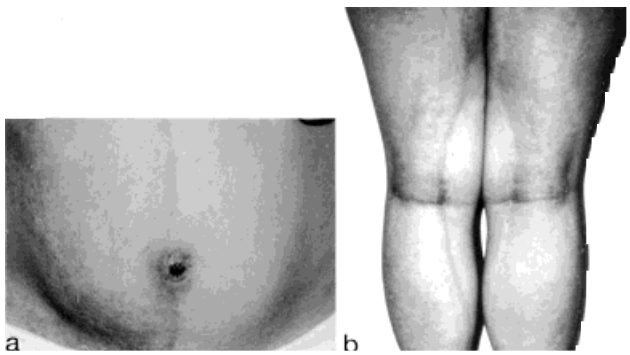

Fig. 1. Hyperpigmented area in the right half of the abdomen with a sharp demarcation on midline (**a**), and linear hyperpigmented areas on the posterior surface of both thighs and legs (**b**).

*Correspondence to: Masahiko Ukita, M.D., Department of Obstetrics and Gynecology, Kurashiki Central Hospital, Miwa 1-1-1, Kurashiki, Okayama 710, Japan.

Received 23 October 1995; Accepted 3 May 1996

is not accessible. The share of trisomic cells in the lymphocytes is not a good measure, in view of the tissue-to-tissue difference in their frequency. However, these concerns are increasingly being superseded by the practice of prenatal diagnosis, for which a previous trisomic baby is an indication.

REFERENCES

Bensen JT, Steele MW (1985): A mildly retarded woman with 46, XX/47, XX, +18 mosaicism. Am J Med Genet 22:343–346.

Beratis NG, Kardon NB, Hsu LYF, Grossman D, Hirschhorn K (1972): Parental mosaicism in trisomy 18. Pediatrics 50:908–911.

Butler MG (1994): Trisomy 18 mosaicism in a 24-year-old white woman with normal intelligence and skeletal abnormalities. Am J Med Genet 53:92–93.

Collins AL, Fisher J, Crolla JA, Cockwell AE (1995): Further case of trisomy 18 mosaicism with a mild phenotype. Am J Med Genet 56:121–122.

Flannery DB (1990): Pigmentary dysplasia, hypomelanosis of Ito, and genetic mosaicism. Am J Med Genet 35:18–21.

Gersdorf E, Utermann B, Utermann G (1990): Trisomy 18 mosaicism in an adult woman with normal intelligence and history of miscarriage. Hum Genet 84:298–299.

Graham DA, Jewitt MM, Fitzgerald PH (1992): Trisomy 18 mosaicism with complete peripheral lymphocyte trisomy and normal intelligence. Clin Genet 41:36–38.

Kohn G, Shohat M (1987): Trisomy 18 mosaicism in an adult with normal intelligence. Am J Med Genet 26:929–931.

Murano I, Ohashi H, Tsukahara M, Tonoki H, Okino F, Atsumi M, Kajii T (1991): Pigmentary dysplasia in long survivors with mosaic trisomy 18: Report of two cases. Clin Genet 39:68–74.

Ohashi H, Tsukahara M, Murano I, Naritomi K, Nishioka K, Miyake S, Kajii T (1992): Pigmentary dysplasias and chromosomal mosaicism: Report of 9 cases. Am J Med Genet 43:716–721.

Sarigol SS, Rogers DG (1994): Trisomy 18 mosaicism in a thirteen-year old girl with normal intelligence, delayed pubertal development, and growth failure. Am J Med Genet 50:94–95.

Thomas IT, Frias J, Cantú ES, Lafer CZ, Flannery DB, Graham JG Jr (1989): Association of pigmentary anomalies with chromosomal and genetic mosaicism and chimerism. Am J Hum Genet 45:193–205.

Masahiko Ukita*
Masaaki Hasegawa
Takashi Nakahori
Department of Obstetrics and Gynecology
Kurashiki Central Hospital
Kurashiki, Japan